


Surveillance of the current situation regarding influenza vaccination according to medical oncologists in Japan

Toshiki Maeda¹  | Hidenori Sasaki² | Atsushi Togawa² | Toshihiro Tanaka² | Hisatomi Arima¹ | Tohru Takata² | Yasushi Takamatsu²

¹Department of Preventive Medicine and Public Health, Faculty of Medicine, Fukuoka University, Fukuoka, Japan

²Department of Oncology, Hematology and Infectious Diseases, Faculty of Medicine, Fukuoka University, Fukuoka, Japan

Correspondence

Toshiki Maeda, Department of Preventive Medicine and Public Health, Faculty of Medicine, Fukuoka University, 8-19-1 Nanakuma, Jonan-ku, Fukuoka 814-0180, Japan.

Email: tmaeda@fukuoka-u.ac.jp

Funding information

Japan Society for the Promotion of Science, Grant/Award Number: 19H03879 and 18K17404

Abstract

This study aimed to clarify the attitude of oncologists toward influenza vaccination and the current situation and issues regarding influenza vaccination for patients on chemotherapy in Japan. A web-based survey of medical oncologists certified by the Japanese Society of Medical Oncology was conducted between November 1 and December 31, 2019. Of the 1369 medical oncologists who were invited to participate, 415 (30.3%) responded to our survey. The questionnaire comprised 4 sections: “oncologist characteristics,” “oncologist attitude toward influenza vaccines and the current status of influenza vaccination for cancer patients undergoing chemotherapy,” “incidence of influenza infection and associated treatment complications,” and “treatment policy for influenza infection.” In total, 153 (36.9%) physicians replied that they did not actively encourage influenza vaccination for patients undergoing chemotherapy. The primary reasons given were lack of evidence (48/153, 31.4%) and uncertainty of appropriate timing (46/153, 30.1%). There was diverse variation in the timing of vaccination and in the levels of encouragement based on the cancer location and medication type. Two hundred eighty-three (68.2%) oncologists reported that their cancer patients had experienced influenza infection while undergoing chemotherapy, and 169 (40.7%) responded that their patients had experienced an administration delay or discontinuation of medication because of influenza infection. Our surveillance revealed some oncologists considered evidence regarding the administration of influenza vaccine to cancer patients undergoing chemotherapy (particularly the optimal timing and level of recommendation by cancer location and medication) to be lacking. It also exposed the adverse impact of influenza infection in cancer patients.

KEYWORDS

chemotherapy, influenza, medical oncologists, prevention, vaccine

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *Cancer Science* published by John Wiley & Sons Australia, Ltd on behalf of Japanese Cancer Association.

1 | INTRODUCTION

Due to its aging society, Japan has experienced a shift from a higher incidence of acute illnesses such as infection to a higher incidence of chronic illnesses such as cancer and other lifestyle-related conditions. Cancer is currently one of the most prevalent illnesses in Japan. It is estimated that 1 in 2 people will suffer from cancer during their lifetime.¹ Since 1981, cancer has been the leading cause of death, and currently approximately 370 000 people die from cancer each year, which indicates that 1 out of 3 deaths is due to cancer.² For cancer patients, infection may not only spoil their quality of life (QOL) but also trigger adverse effects associated with chemotherapy. Patients with cancer are especially vulnerable to infections because of their weakened immune responses resulting from the cancer itself as well as the treatment.^{3,4} Consequently, some infections are more serious in cancer patients compared with in healthy people and can even be fatal. In addition to the physical distress caused by infections, an extra financial burden,⁵ and interference with ongoing chemotherapy⁶ can also be consequences of infection in cancer patients. Thus, effective prevention and containment of infection are particularly important for people with cancer, especially given the currently ongoing global pandemic of coronavirus disease 2019 (COVID-19).

One of the most troublesome infections in Japan, as in many other countries, is influenza virus infection. Like COVID-19, influenza is a febrile illness. Because distinguishing influenza from COVID-19 on the basis of clinical symptoms alone is challenging, the current global pandemic of COVID-19 makes the containment of influenza a particularly urgent issue. In Japan, it is estimated that 12 million people visited a health care facility because of influenza in 2019, with 20 389 of those people admitted onto wards, resulting in 3400 excess deaths.⁷ A study from the USA reported that the hospitalization rate among those with cancer was higher than that of the general population and that 9% of hospitalized patients with cancer were estimated to die from influenza-related infections.⁸ Therefore, influenza is considered a critical source of morbidity and mortality among cancer patients.⁹

At present, influenza, unlike COVID-19, can be prevented by vaccination. According to a Cochrane systematic review, influenza vaccinations have reduced the incidence of influenza infection by approximately 60% in the general population.¹⁰ Regarding cancer patients, 1 study conducted among patients with colorectal cancer, which is one of the most prevalent types of cancer in Japan, reported that influenza vaccination significantly decreased pneumonia development, all-cause mortality, and chemotherapy discontinuation.¹¹ However, the effectiveness of influenza vaccination for individuals with cancer is somewhat unclear when compared with its effectiveness for immunocompetent people because of the small sample sizes and methodological limitations of the studies conducted on this population.^{3,9,12} Research performed outside Japan found low rates of influenza vaccination among those with cancer, stemming from uncertainty about its effectiveness, fear of side effects, and a lack of data regarding

the appropriate timing for vaccine administration.^{13,14} Because patients in Japan tend to be dependent and passive, and they have few opportunities to participate in medical decision-making,¹⁵ the physician's attitude toward influenza vaccination is very likely to influence their patient's behavior. To date, few studies have systematically surveyed medical oncologists' attitudes toward influenza vaccination and the current situation and issues related to influenza vaccination for cancer patients undergoing chemotherapy.

The aim of the present study was to clarify the attitude of oncologists in Japan toward influenza vaccination for cancer patients and the current situation and issues of influenza vaccination for cancer patients undergoing chemotherapy by conducting a web-based surveillance of medical oncologists in Japan. The findings of this work may provide direction for future research aimed at improving the QOL of cancer patients.

2 | MATERIALS AND METHODS

2.1 | Data collection and participants

A web-based surveillance of medical oncologists was conducted as part of a comprehensive project to investigate issues related to influenza vaccination for cancer patients (INFLUENZA vaccination for CancEr patients: INFLUENCE project). With the support of the office of the Japanese Society of Medical Oncology (JSMO), 1369 board-certified medical oncologists of JSMO for whom a valid email address was available, which is the group of all eligible oncologists, were invited to participate in the present surveillance. The surveillance period was from November 1 to December 31, 2019. The information was collected anonymously using a web-based data collection system (SurveyMonkey). Before data collection, web-based, appropriate consent was obtained from each participant. This study was approved by the Fukuoka University Clinical Research and Ethics Center (FU-CREC) (U19-304).

2.2 | Questionnaire contents

The survey was created by a team comprised 3 board-certificated physicians who specialize in medical oncology, 2 board-certificated physicians who specialize in infectious diseases, and 1 epidemiology expert. The questionnaire comprised 27 questions, split into the following 4 sections: "oncologist characteristics," "oncologist attitude toward influenza vaccines and the current situation of influenza vaccination for cancer patients undergoing chemotherapy," "incidence of influenza infection and associated treatment complications," and "treatment policy for influenza infection." The "oncologist characteristics" section comprised questions regarding the oncologist's sex, age, number of years practicing oncology (<5, 5-9, 10-19, or ≥ 20 years), specialty (internist, surgeon, pediatrics, or other), annual total number of cancer patients undergoing outpatient

chemotherapy at their institution (<2000, 2000-4999, 5000-9999, or ≥10 000 patients/year), and type of cancer on which they mainly conduct chemotherapy (brain, head, and neck, lung, breast, gastrointestinal, genitourinary, gynecologic, skin, hematology, bone and soft tissue, or pediatric). The “oncologist attitude toward influenza vaccines and the current situation of influenza vaccination for cancer patients undergoing chemotherapy” section comprised questions regarding the degree of recommendation for influenza vaccinations and the corresponding reasons, vaccination timing, the effects of cancer and medication type on their recommendation for influenza vaccination, number of vaccine administrations (1 or 2 shots), and family member vaccination. The “incidence of influenza infection and associated treatment complications” section comprised questions regarding their experiences of influenza infection, infection-related death, and chemotherapy discontinuation among their cancer patients over the past year, their treatment strategy, and how they manage and collect information from their patients with influenza. The “treatment policy for influenza infection” section comprised questions regarding the attitude of medical oncologists toward anti-influenza drug use and the associated reasons and the drug they use most often for anti-influenza treatment.

2.3 | Statistical analysis

The results of the questionnaire were transferred into Excel format, and Excel and STATA release 16 (STATA Corp, College Station, TX, USA) were used to calculate and summarize the data. The number in each response category was divided by the number of valid responses to obtain the frequency. We also obtained 95% confidence intervals for the responses to key questions and the associated reasons.

3 | RESULTS

3.1 | Oncologist characteristics

We distributed the questionnaire to 1369 medical oncologists and received responses from 415 (30.3%). Table 1 lists the demographics and characteristics of the responding medical oncologists. Most (82.4%) of the responding medical oncologists were men, and approximately half of the respondents were aged 40-49 y. The majority (89.6%) of the responding medical oncologists were internists. As for the total number of their patients having outpatient chemotherapy per year, 97 (23.4%) of the responding medical oncologists answered with < 2000 patients/year, 106 (25.5%) answered with 2000-4999 patients/year, 114 (27.5%) answered with 5000-9999 patients/year, and 98 (23.6%) answered with ≥10 000 patients/year. Many of the responding medical oncologists treated patients with gastrointestinal cancer (226 [54.5%]), lung cancer (158 [38.1%]), breast cancer (130 [31.3%]), or bone and soft tissue cancer (129 [31.1%]).

TABLE 1 Characteristics of the responding medical oncologists

	N	%
Sex		
Male	342	82.4
Age		
<40 y	76	18.3
40-49 y	207	49.9
50-59 y	116	28.0
>60 y	16	3.9
Length of time working as an oncologist		
<5 y	5	1.2
5-9 y	59	14.2
10-19 y	191	46.0
>20 y	160	38.6
Specialty		
Internal medicine	372	89.6
Surgery	39	9.4
Pediatrics	1	0.2
Other	3	0.7
Annual number of outpatient chemotherapy patients in their institution		
<2000	97	23.4
2000-4999	106	25.5
5000-9999	114	27.5
≥10 000	98	23.6
Type of cancer treated		
Brain	16	3.9
Head and neck	115	27.7
Lung	158	38.1
Breast	130	31.3
GI tract	226	54.5
Urogenital	72	17.4
OB-Gy	77	18.6
Skin	58	14.0
Blood	114	27.5
Bone and soft tissue	129	31.1
Pediatric	4	1.0

Abbreviations: GI, gastrointestinal; OB-GY, obstetrics and gynecology.

3.2 | Key questions and corresponding answers

3.2.1 | Oncologist attitude toward influenza vaccines and the current situation of influenza vaccination for cancer patients undergoing chemotherapy

“Do you recommend patients undergoing chemotherapy to get an influenza vaccine?”

For this question, 241 (58.1%) replied with “I recommend it to almost

everyone," 143 (34.5%) replied with "I support it if the patient asks," and 10 (2.4%) replied with "I do not actively recommend it" (Table 2). Among the 241 responding medical oncologists who answered "I recommend it to almost everyone," 214 respondents (88.8%) reported that they did so "to prevent influenza infection from getting worse" and 104 respondents (43.2%) reported that they did so "to prevent the onset of influenza infection." Among the 153 responding medical oncologists who answered with "I support it if the patient asks" or "I do not actively recommend it," 48 (31.4%) and 46 (30.1%) reported that they did not proactively encourage vaccination because of "lack of evidence" and "uncertainty of appropriate timing," respectively (Table 3).

"When is the appropriate timing for receiving the influenza vaccine?"

We asked the 384 oncologists who claimed "I recommend it to almost everyone" or "I support it if the patient asks" about the appropriate timing of influenza vaccine administration. Among them, 157 (40.9%) answered with "I do not particularly care about timing," 94 (24.5%) answered with "between chemotherapy treatments (after chemotherapy has been discontinued)," and 82 (21.4%) answered with "during chemotherapy" (Table 2). In the freeform answers, an opinion such as "any time other than during the bone marrow suppression phase" was frequently found.

"How many influenza vaccine administrations do you recommend cancer patients to receive?"

We also asked the 384 medical oncologists who claimed "I recommend it to almost everyone" or "I support it if the patient asks" about the number of influenza vaccine administrations they recommend. Almost all of them (362 [94.3%]) responded that they recommended just 1 shot (Table 2).

"Do you change your degree of recommendation for influenza vaccination depending on the patient's cancer type?"

Regarding changes in their degree of recommendation for influenza vaccination related to the patient cancer type, 74 of the responding medical oncologists (17.8%) answered with "Yes, I change my degree of recommendation" and 326 (78.6%) replied with "No, I do not change my degree of recommendation" (Table 2). The 74 oncologists who answered with "Yes, I change my degree of recommendation" were asked for what cancer types they particularly recommend patients get the influenza vaccine; 38 (51.4%) answered with malignant lymphoma, 30 (40.5%) answered with multiple myeloma, 28 (37.8%) answered with small cell lung cancer, 26 (35.1%) answered with acute leukemia, 26 (35.1%) answered with chronic leukemia, and 24 (32.4%) answered with non-small cell lung cancer. Notably, several physicians specifically discouraged patients with malignant lymphoma (21 [28.4%]), acute leukemia (20 [27.9%]), or multiple myeloma (15 [20.3%]) from getting an influenza vaccine (Table 4).

"Do you change your degree of recommendation for influenza vaccination depending on the type of chemotherapy medication?"

For this question, 122 (29.4%) oncologists responded with "Yes, I change my recommendation," whereas 270 (65.1%) oncologists replied

with "No, I do not change my recommendation" (Table 2). We asked the 122 medical oncologists who responded with "Yes, I change my degree of recommendation" what type of medication they regarded as influencing their recommendation for influenza vaccination. Many physicians recommended vaccination for patients receiving cytotoxic anti-cancer drugs (91 [74.6%]), small molecule compounds (57 [46.7%]), and antibodies (56 [45.9%]). However, 59 (48.3%) respondents did not recommend influenza vaccination for patients receiving immune checkpoint inhibitors. In the freeform answers, responses along the lines of "I discourage influenza vaccination during chemotherapy with corticosteroids and rituximab" were frequently found (Table 5).

"Do you also recommend patient family members to get vaccinated against influenza?"

In response to the above question, 204 oncologists (54.0%) answered positively ("I recommend it to almost everyone" or "I sometimes recommend it"), whereas 168 (40.5%) answered negatively ("I do not recommend it very much," "I rarely recommended it," or "I never recommend it" (Table 2).

3.3 | Incidence of influenza infection and associated treatment complications

3.3.1 | "Have you experienced any patients suffering from influenza in the last year?" and "have you experienced cases in which influenza infection caused a delay or discontinuation of chemotherapy in the last year?"

Of the 415 responding medical oncologists who answered the question "have you experienced any patients suffering from influenza in the last year?", 283 (68.2%) answered with "yes" (Table 2). In addition, 169 (40.7%) physicians reported experiencing a delay or discontinuation of chemotherapy in their patients because of influenza infection.

3.4 | Treatment policy for influenza infection

3.4.1 | "What is the treatment strategy for patients who have contracted influenza during chemotherapy?"

Regarding the treatment policy for influenza infection during chemotherapy, 339 of the 415 responding oncologists (81.7%) answered with "I prescribe anti-influenza drugs proactively." In contrast, 29 (7.0%) oncologists responded with "I prescribe anti-influenza drugs if the patient asks," and 3 (0.7%) replied with "I do not prescribe anti-influenza drugs as much as possible" (Table 2). When we asked the 339 medical oncologists who responded with "I prescribe anti-influenza drugs proactively" why they did so, 284 (83.8%) physicians selected "to prevent influenza infection from getting worse" and 233 (68.7%) replied with "for rapid improvement of their symptoms." Oseltamivir (284 [68.4%]) and laninamivir (184 [44.3%]) were frequently used

TABLE 2 Key survey questions and corresponding answers

Survey questions and corresponding answers	N	% (95% CI)
<i>Oncologist attitude toward influenza vaccines and the current situation of influenza vaccination for cancer patients undergoing chemotherapy</i>		
Do you recommend patients undergoing chemotherapy to get an influenza vaccine? (N = 415)		
I recommend it to almost everyone	241	58.1 (53.3-62.8)
I support it if the patient asks	143	34.5 (29.9-39.0)
I do not actively recommend it	10	2.4 (0.9-3.9)
When is the appropriate timing for receiving the influenza vaccine? (subjects: those who answered with "I recommend it to almost everyone" or "I support it if the patient asks" (N = 384))		
Between chemotherapy treatments (after chemotherapy has been discontinued)	94	24.5 (20.2-28.8)
During chemotherapy	82	21.4 (17.3-25.5)
I do not particularly care about timing	157	40.9 (36.0-45.8)
How many influenza vaccine administrations do you recommend cancer patients to receive? (subjects: those who answered with "I recommend it to almost everyone" or "I support it if the patient asks" (N = 384))		
One	362	94.3 (91.9-96.6)
Two	6	1.6 (0.3-2.8)
Do you change your degree of recommendation for influenza vaccination depending on the patient's cancer type? (N = 415)		
Yes, I change my degree of recommendation	74	17.8 (14.1-21.5)
No, I do not change my degree of recommendation	326	78.6 (74.6-82.5)
Do you change your degree of recommendation for influenza vaccination depending on the type of chemotherapy medication? (N = 415)		
Yes, I change my degree of recommendation	122	29.4 (25.0-33.8)
No, I do not change my degree of recommendation	270	65.1 (60.5-69.6)
Do you also recommend patient family members to get vaccinated against influenza? (N = 415)		
I recommend it to almost everyone	160	38.6 (29.9-47.2)
I sometimes recommend it	64	15.4 (9.0-21.8)
I do not recommend it very much	105	25.3 (17.6-33.0)
I rarely recommended it	61	14.7 (8.4-21.0)
I never recommend it	2	0.5 (0.0-1.7)
<i>Incidence of influenza infection and associated treatment complications</i>		
Have you experienced any patients suffering from influenza in the last year? (N = 415)		
Yes	283	68.2 (63.7-72.7)
No	96	23.1 (19.0-27.2)
Have you experienced cases in which influenza infection caused a delay or discontinuation of chemotherapy in the last year? (N = 415)		
Yes	169	40.7 (36.0-45.4)
No	210	50.6 (45.8-55.4)
<i>Treatment policy for influenza infection</i>		
What is the treatment strategy for patients who have contracted influenza during chemotherapy?		
I prescribe anti-influenza drugs proactively	339	81.7 (78.0-85.4)
I prescribe anti-influenza drugs if the patient asks	29	7.0 (4.5-9.4)
I do not prescribe anti-influenza drugs as much as possible	3	0.7 (0.0-1.5)
Type of medication you use (multiple answers were allowed)		
Oseltamivir	284	68.4 (64.0-72.9)
Zanamivir	88	21.2 (17.3-25.1)
Laninamivir	184	44.3 (39.6-49.1)
Peramivir	53	12.8 (9.6-16.0)
Baloxavir	36	8.7 (6.0-11.4)

Note: Physicians who answered with "other" or provided no response were excluded from the table; consequently, the total percentage is not always 100%.

TABLE 3 Reasons why chemotherapy medical oncologists recommend or do not recommend influenza vaccination

Reasons (multiple answers were allowed)	N	% (95% CI)
Why do you recommend influenza vaccine? (subjects: those who answered with "I recommend it to almost everyone" (N = 241))		
To prevent the onset of influenza infection	104	43.2 (36.9-49.4)
To prevent influenza infection from getting worse	214	88.8 (84.8-92.8)
It is recommended in the guidelines	58	24.1 (18.7-29.5)
Policy of health care facility or department	11	4.6 (1.9-7.2)
Why do you not recommend influenza vaccine? (subjects: those who answered with "I support it if the patient asks" or "I do not actively recommend it" (N = 153))		
Low expectation for an effect	27	17.6 (11.6-23.7)
Lack of evidence	48	31.4 (24.0-38.7)
Worry about adverse effects	24	15.7 (9.9-21.4)
It interferes with chemotherapy	3	2.0 (0.0-4.2)
Uncertainty of appropriate timing	46	30.1 (22.8-37.3)
Increased cost for patients	13	8.5 (4.1-12.9)
Policy of health care facility or department	3	2.0 (0.0-4.2)

Note: Physicians who answered with "other" or provided no response were excluded from the table; consequently, the total percentage is not always 100%.

as anti-influenza drugs. When we asked the 34 physicians who answered with "I prescribe anti-influenza drugs if the patient asks," or "I do not prescribe anti-influenza drugs as much as possible" for reason they did not proactively prescribe anti-influenza drugs to their patients, the most common replies were the low efficacy of the drugs (9 [28.1%]) and a lack of evidence (9 [28.1%]) (Table 6).

4 | DISCUSSION

4.1 | Chief finding of the study

The present study conducted a questionnaire survey to clarify the current situation and issues relating to influenza vaccination among patients undergoing chemotherapy in Japan. We found that many of the responding medical oncologists recommend their patients to get an influenza vaccine while undergoing chemotherapy. The reason they provided for recommending influenza vaccination was to prevent infection and to limit infection severity. A few medical oncologists reported that they do not recommend their patients to be vaccinated against influenza because of the limited evidence on the efficacy and appropriate timing of the influenza vaccine in cancer patients. There was a large variety of opinions among medical oncologists regarding the

TABLE 4 Type of cancer medical oncologists who recommend or do not recommend influenza vaccination

Cancer type	N	% (95%CI)
Cancer types for which influenza vaccination is recommended (subjects: those who answered yes when asked "do you change your degree of recommendation for influenza vaccination depending on the patient's cancer type?" (N = 74)) (multiple answers were allowed)		
Brain tumor	11	14.9 (6.8-23.0)
Head and neck tumors	13	17.6 (8.9-26.2)
Small cell lung cancer	28	37.8 (26.8-48.9)
Non-small cell lung cancer	24	32.4 (21.8-43.1)
Breast cancer	17	23.0 (13.4-32.6)
Esophageal cancer	12	16.2 (7.8-24.6)
Gastric cancer	13	17.6 (8.9-26.2)
Colon and rectal cancer	14	18.9 (10.0-27.8)
Liver cancer	10	13.5 (5.7-21.3)
Bile and pancreatic cancer	11	14.9 (6.8-23.0)
Renal urinary tract cancer	9	12.2 (4.7-19.6)
Prostate cancer	11	14.9 (6.8-23.0)
Uterine cancer	9	12.2 (4.7-19.6)
Ovarian cancer	11	14.9 (6.8-23.0)
Acute leukemia	26	35.1 (24.3-46.0)
Chronic leukemia	26	35.1 (24.3-46.0)
Malignant lymphoma	38	51.4 (40.0-62.7)
Multiple myeloma	30	40.5 (29.4-51.7)
Skin cancer	9	12.2 (4.7-19.6)
Bone and soft tissue tumors	14	18.9 (10.0-27.8)
Germ cell tumors	16	21.6 (12.2-31.0)
Cancer type for which influenza vaccination is not recommended (subjects: those who answered yes when asked "Do you change your degree of recommendation for influenza vaccination depending on the patient's cancer type?" (N = 74)) (multiple answers were allowed)		
Brain tumor	3	4.1 (0.0-8.5)
Head and neck tumors	1	1.4 (0.0-4.0)
Small cell lung cancer	0	0.0 (n/a)
Non-small cell lung cancer	3	4.1 (0.0-8.5)
Breast cancer	1	1.4 (0.0-4.0)
Esophageal cancer	1	1.4 (0.0-4.0)
Gastric cancer	1	1.4 (0.0-4.0)
Colon and rectal cancer	2	2.7 (0.0-6.4)
Liver cancer	3	4.1 (0.0-8.5)
Bile and pancreatic cancer	1	1.4 (0.0-4.0)
Renal urinary tract cancer	1	1.4 (0.0-4.0)
Prostate cancer	3	4.1 (0.0-8.5)
Uterine cancer	1	1.4 (0.0-4.0)
Ovarian cancer	1	1.4 (0.0-4.0)
Acute leukemia	20	27.0 (16.9-37.1)

(Continues)

TABLE 4 (Continued)

Cancer type	N	% (95%CI)
Chronic leukemia	7	9.5 (2.8-16.1)
Malignant lymphoma	21	28.4 (18.1-38.7)
Multiple myeloma	15	20.3 (11.1-29.4)
Skin cancer	3	4.1 (0.0-8.5)
Bone and soft tissue tumor	1	1.4 (0.0-4.0)
Germ cell tumors	1	1.4 (0.0-4.0)

Note: Physicians who answered with "other" or provided no response were excluded from the table; consequently, the total percentage is not always 100%.

TABLE 5 Type of medication chemotherapy medical oncologists recommend or do not recommend influenza vaccination

Medication type	N	% (95%CI)
Medications associated with recommending influenza vaccination (subjects: those who answered yes when asked "do you change the degree of recommendation for influenza vaccination depending on the type of chemotherapy medication?" (N = 122))		
Cytotoxic anti-cancer drugs	91	74.6 (66.9-82.3)
Endocrine drugs	46	37.7 (29.1-46.3)
Antibodies	56	45.9 (37.1-54.7)
Small molecular compounds	57	46.7 (37.9-55.6)
Immune checkpoint inhibitors	20	16.4 (9.8-23.0)
Medications associated with not recommending influenza vaccination (subjects: those who answered yes when asked "do you change the degree of recommendation for influenza vaccination depending on the type of chemotherapy medication?" (N = 122))		
Cytotoxic anti-cancer drugs	10	8.2 (3.3-13.1)
Endocrine drugs	14	11.5 (5.8-17.1)
Antibodies	22	18.0 (11.2-24.9)
Small molecular compounds	6	4.9 (1.1-8.8)
Immune checkpoint inhibitors	59	48.4 (39.5-57.2)

Note: Physicians who answered with "other" or provided no response were excluded from the table; consequently, the total percentage is not always 100%.

appropriate timing of vaccination and the degree of either encouragement or discouragement of the influenza vaccine based on the types of cancer, especially hematologic malignancy, and the types of medication used in the patient's chemotherapy regimen. Approximately 40% of medical oncologists did not actively encourage family members of their patients to be vaccinated. Approximately 70% of medical oncologists experienced influenza infections among their patients in the previous year, and 40% of medical oncologists experienced a discontinuation of chemotherapy resulting from influenza infection.

4.2 | The effectiveness of influenza vaccination

A systematic review by Demicheli et al found that the incidence of influenza infection was reduced by approximately 60% in healthy

TABLE 6 Rationale for using or not using antiviral drugs to treat influenza infection in cancer patients

Reasons (multiple answers were allowed)	N	% (95%CI)
Reasons oncologists proactively prescribe anti-influenza drugs (subjects: those who answered with "I prescribe anti-influenza drugs proactively" (N = 339))		
To prevent influenza infection from getting worse	284	83.8 (79.9-87.7)
For rapid improvement of their symptoms	233	68.7 (63.8-73.7)
Patients or family requested them	40	11.8 (8.4-15.2)
To prevent delays in chemotherapy	73	21.5 (17.2-25.9)
Reasons oncologists do not proactively prescribe anti-influenza drugs (subjects: those who answered with "I prescribe anti-influenza drugs if the patient asks" or "I do not prescribe anti-influenza drugs as much as possible" (N = 32))		
Low expectation for an effect	9	28.1 (12.6-43.7)
There is no evidence	9	28.1 (12.6-43.7)
Worry about adverse effects	3	9.4 (0.0-19.5)
Worry about interactions between the vaccine and chemotherapy	4	12.5 (1.0-24.0)
Increased cost for patients	1	3.1 (0.0-9.2)

Note: Physicians who answered with "other" or provided no response were excluded from the table; consequently, the total percentage is not always 100%.

people who were vaccinated against influenza virus.¹⁰ Due to comorbidities, such as malignancy, or medications, including chemotherapy, immunocompromised persons are at relatively higher risk for experiencing medical complications from severe influenza.¹⁶ Therefore, guidelines recommend that immunocompromised persons be vaccinated against influenza.^{16,17} Although these guidelines strongly recommend influenza vaccination for such patients, the supporting evidence for this recommendation is somewhat weak. There are few studies reporting the clinical effectiveness of influenza vaccines among cancer patients who are receiving chemotherapy, and many studies on influenza vaccination in this population employed antibody responses as a surrogate marker of vaccine effectiveness.¹⁸ Earle et al evaluated the clinical effectiveness of influenza vaccination for patients with colorectal cancer who were undergoing chemotherapy and found significant decreases in pneumonia development, all-cause mortality, and chemotherapy discontinuation.¹¹ A systematic review that included this study by Earle et al reported a significant reduction in mortality among the influenza vaccine group, although the number of observations was small, and the evidence level was assessed as being weak.¹⁹ Based on a relatively large-scale population-based study employing a test negative design, Blanchette et al reported that the effectiveness of influenza vaccination in cancer patients was approximately 20%; however, details on the concurrent medications, chemotherapy

regimens, and vaccination timing were not specified.¹² Therefore, although the available data suggest that influenza vaccination among cancer patients undergoing chemotherapy may have some positive effect, the evidence on its effectiveness is still insufficient. The present study demonstrates that approximately 40% of medical oncologists do not actively encourage vaccination, in part because of uncertainty regarding the effectiveness of influenza vaccination in cancer patients.

4.3 | The optimal timing of influenza vaccination

It usually takes *c.* 2 wk for specific antibodies to emerge after inoculation with an influenza vaccine.²⁰ The optimal timing of influenza vaccine administration is controversial, and there are various opinions regarding the appropriate timing of vaccination during chemotherapy. Ortals et al compared the antibody response between patients vaccinated against influenza at the start of the chemotherapy with those vaccinated against influenza at the nadir phase among patients with various types of cancer (solid tumors and hematologic malignancies), and they reported that a significantly higher proportion of the patients who were vaccinated at the nadir phase developed influenza-specific antibodies.²¹ Wumkeset et al performed a randomized control trial (RCT) to compare antibody responses to influenza vaccination between patients vaccinated on day 5 and those vaccinated on day 16 of adjuvant chemotherapy for breast or colon cancer. A significantly higher response was observed in the breast cancer patients who were vaccinated on day 5 compared with those who were vaccinated on day 16, whereas no significant difference was found between the corresponding 2 groups of colon cancer patients.²² Keam et al compared influenza vaccinations on day 1 and day 11 in lung or breast cancer patients on a 3-wk cycle of chemotherapy, and they reported that the timing of vaccination made no significant difference for antibody production.²³ There have been various published recommendations on the timing of influenza vaccination, such as 2 wk before the start of chemotherapy,^{17,24-26} 1 mo after chemotherapy, and when the amount of white blood cells has recovered to more than 1000 cells/mm.²⁷ The answers provided by the medical oncologists who answered our survey were split regarding recommending influenza vaccination between chemotherapy cycles or during chemotherapy; this suggests that there is currently no established consensus about the timing of influenza vaccination. Thus, further research on the optimal timing of influenza vaccination in cancer patients undergoing chemotherapy is needed.

4.4 | The difference in influenza vaccine efficacy among cancer types

Some studies have reported that the efficacy of influenza vaccination in particular subsets of cancer patients, such as those with lung cancer²⁸ or breast cancer,^{22,29} is equivalent to that in healthy people. In contrast, other studies have shown that the response to influenza vaccination is poor in patients with a hematologic malignancy such as

multiple myeloma (MM) or non-Hodgkin lymphoma.^{12,25,26,30} The present work found that approximately 20% of medical oncologists do not recommend influenza vaccination to patients with a hematologic malignancy, specifically malignant lymphoma (ML), acute leukemia, or MM. As stated above, the effectiveness of influenza vaccination in cancer patients, especially those with a hematologic malignancy, is controversial. Further studies are needed to determine the most effective management for cancer patients, especially those with a hematologic malignancy, regarding potential influenza infection.

4.5 | Medications potentially associated with a poor response to influenza vaccination

This study revealed that some medical oncologists do not endorse influenza vaccination for patients who are undergoing treatment with corticosteroids, rituximab, or immune checkpoint inhibitors. Corticosteroids impair the immune function of non-lymphoid and lymphoid cells via exerting direct effects on gene transcription.⁴ The influence of corticosteroids on the efficacy of influenza vaccination is ambiguous. Some studies have reported that the level of specific anti-influenza virus antibodies is significantly increased after receiving influenza vaccination, both in patients with systemic lupus erythematosus (SLE) or rheumatoid arthritis who are receiving corticosteroids and in healthy subjects,^{31,32} whereas others have shown that the immune response to influenza vaccination in patients with SLE is lower compared with that in the general population.^{33,34} Notably, there was wide variance in the dose and duration of corticosteroid treatment as well as in the underlying illness of subjects; thus, it could be difficult to determine the efficacy of influenza vaccination in this group.

Rituximab induces B-cell depletion via complement and antibody-dependent cellular cytotoxicity at 24-48 h after infusion. It takes 6 mo to recover peripheral blood B-lymphocytes,³⁵ and it takes up to 1 y for these cells to return to their pretreatment levels.³⁶ Many studies have reported poor responses to influenza vaccination in patients who were treated with a rituximab-containing regimen.³⁷⁻³⁹ Immune checkpoint inhibitors exert an antitumor effect by blocking inhibitors of T-cell activation, such as programmed cell death protein 1 (PD-1), programmed death ligand 1 (PD-L1), and cytotoxic T-lymphocyte associated protein 4 (CTLA4).⁴⁰ Although a small study from Switzerland found that the frequency of immune-related adverse effects (irAEs) increased after influenza vaccination in cancer patients receiving immune checkpoint inhibitors,⁴¹ more recent studies have indicated that influenza vaccination does not induce irAEs in these patients.^{40,42} However, evidence that clarifies the efficacy and safety of influenza vaccination in cancer patients receiving chemotherapy, such as rituximab and immune checkpoint inhibitors, remains insufficient; therefore further studies are needed.

4.6 | Other considerations

Almost all the responding medical oncologists who support influenza vaccination of cancer patients indicated that they recommended

their patients have a single administration of influenza vaccine. Their recommendations are in agreement with those of the Advisory Committee on Immunizations (ACIP), which does not recommend 2 doses of influenza vaccine.¹⁷ However, the ACIP recommendation was derived from the results of 1 well designed small RCT³⁸ and studies conducted on patients with HIV^{9,43,44}; therefore reliable evidence on this topic is still lacking, and further large-scale studies are desirable.

Influenza is often transmitted to cancer patients from their family members, therefore it is important for patient family members to also get vaccinated against influenza to help prevent them from infecting the patient.⁴⁵ In guidelines published by the Infectious Diseases Society of America, influenza vaccination of cancer patient family members is also strongly recommended.¹⁷ However, our survey revealed that approximately 40% of medical oncologists do not actively encourage the family members of patients to receive influenza vaccination. Because it is important for medical oncologists to recommend influenza vaccination not only for their cancer patients but also for their patients' families, this finding highlights an important clinical gap that should be addressed.

There have been no RCTs to examine the efficacy of anti-influenza agents in cancer patients; the responding medical oncologists reported using neuraminidase inhibitors such as oseltamivir, zanamivir, or peramivir, based on United States Food and Drug Administration approval.⁴⁶ According to the results of a previous survey conducted on 200 physicians in Japan via a commercial magazine, many physicians (about 80%) prescribed oseltamivir and laninamivir in 2017-2018, after which the trend changed, and the prescription rate for baloxavir increased up to 30% in 2019. In agreement with this prior survey, the responding medical oncologists in the present study also reported prescribing oseltamivir and laninamivir. However, <10% of our survey respondents reported prescribing baloxavir. Although the emergence of baloxavir-resistant influenza virus has been reported recently,⁴⁷ the prophylactic effect of baloxavir on household contacts has also been reported.⁴⁸ Further studies are desired to uncover the optimum use of anti-influenza drugs among cancer patients.

4.7 | Strengths and limitations

The main strength of this study is that we surveyed medical oncologists throughout Japan and asked them comprehensively about their current situation. We examined the attitude of physicians toward influenza vaccination of cancer patients and their families along with the current situation and vaccination issues for influenza, which provides a baseline of doctor behaviors and attitudes just before the COVID-19 pandemic in Japan. The main limitations of this work are as follows: (1) the response rate was only 30% out of all registered medical oncologists; (2) this survey was conducted anonymously, so the reliability of the provided answers is uncertain; and (3) because we surveyed physicians rather than their patients, we could not obtain accurate numbers of cancer

patients who received an influenza vaccine or contracted an influenza infection.

4.8 | Future perspectives

Due to the currently ongoing global pandemic of COVID-19, containment of influenza is an urgent public health issue. Our research clarifies the baseline of physician attitude toward influenza vaccination of cancer patients and the current situation and vaccination issues for influenza, which will be helpful for measuring and managing influenza infection in the present COVID-19 era. Based on the results of our influenza questionnaire, we reviewed various studies, which revealed some contrasting reports regarding influenza vaccination among cancer patients, specifically in relation to the timing of influenza vaccine administration and the types of cancers and medications for which influenza vaccination is effective. At present, many studies recommend cancer patients undergoing chemotherapy to receive influenza vaccination^{25,29} because there are few reports of major adverse events caused by influenza vaccines.^{9,49} Because previous studies have shown that the influenza-specific antibody level rose after vaccination to a sufficient level in solid tumor patients, in a manner identical to that of healthy people, influenza vaccination should be recommended for those with a solid tumor.^{28,29} However, the effect of influenza vaccination among those with a hematologic malignancy, such as ML or MM, has not been determined to date because the sample sizes of relevant studies were small and the populations of some studies were composed of patients with mixed cancer types (solid tumor and hematologic malignancy). Therefore, additional large-scale studies, particularly those focused on hematologic malignancy, are needed. In addition, further studies are also needed to investigate the appropriate timing and dose number for influenza vaccination and to verify the effectiveness of influenza vaccination in patients undergoing treatment with rituximab or novel anti-cancer drugs, such as immune checkpoint inhibitors. Ideally, the endpoint of such studies should be clinical responses, such as reductions in the rates of infection and mortality, rather than serological responses. However, in an influenza vaccine study, an extremely large number of patients would be needed because of the low occurrence of infection. Furthermore, conducting an RCT might be unethical if patients in the control arm were not given any vaccine. To overcome these issues, the design employed by Blanchette et al, in which vaccination history was linked to large-scale hospital administrative data, could be useful.¹² In Japan, insurance claim data, which has long been used for payment, has recently become available for research. It contains information on the type of medication and day of its administration, hence a more detailed study could be possible if the claim data were linked to vaccination history. However, information on vaccination is not currently available. To improve the QOL of cancer patients, the disclosure of vaccine information for enabling further detailed study in Japan is desirable.

5 | CONCLUSION

We conducted a national surveillance of medical oncologists in Japan using a web-based questionnaire to clarify the current situations and issues relating to influenza vaccination among cancer patients who were undergoing chemotherapy. The present study demonstrated that approximately 40% of medical oncologists do not actively encourage influenza vaccination for cancer patients and their families, in part because of uncertainty regarding the effectiveness of influenza vaccination in cancer patients. Opinions regarding the timing of influenza vaccination and the types of cancers and medications for which to recommend influenza vaccination varied among the surveyed medical oncologists. Approximately 70% of the responding medical oncologists reported that they had experienced a case of influenza infection among their patients, and 40% of these medical oncologists had experienced a case in which chemotherapy was discontinued because of influenza infection. The available data regarding influenza vaccination among cancer patients, especially those with a hematologic malignancy or who were being treated with certain medications, are insufficient. To improve the QOL of cancer patients, the disclosure of vaccine information for enabling further detailed studies in Japan is desirable.

ACKNOWLEDGMENTS

We thank Hiromi Nishizawa (secretary of the JSMO) for conducting the online survey and collecting the data. We thank Katie Oakley, PhD, from Edanz Group (<https://en-author-services.edanzgroup.com/ac>), for editing drafts of this manuscript. HA received research grants from Daiichi Sankyo and Takeda, lecture fees from Bayer, Daiichi Sankyo, Fukuda Denshi, MSD, Takeda, and Teijin, and fees for consultancy from Kyowa Kirin. This work was supported by JSPS KAKENHI grant numbers 18K17404 and 19H03879.

CONFLICT OF INTEREST

There is no conflict of interest to be declared.

ORCID

Toshiki Maeda  <https://orcid.org/0000-0002-5634-9792>

REFERENCES

1. CANCER STATISTICS IN JAPAN '18 [Cancer information Service, National Cancer Center Japan] [Internet]. [cited 2020 May 1]. Available from: https://ganjoho.jp/en/professional/statistics/brochure/2018_en.html
2. Health Labour and Welfare Statistic Association. *Journal of Health and Welfare Statistics 2019/2020* [Internet]; 2019. [cited 2020 May 1]. Available from: <https://www.amazon.co.jp/dp/B07VDMP7Q8>
3. Pedrazzoli P, Baldanti F, Donatelli I, et al. Vaccination for seasonal influenza in patients with cancer: Recommendations of the Italian Society of Medical Oncology (AIOM). *Ann Oncol*. 2014;25(6):1243-1247.
4. Kunisaki KM, Janoff EN. Influenza in immunosuppressed populations: a review of infection frequency, morbidity, mortality, and vaccine responses. *Lancet Infect Dis*. 2009;9(8):493-504.
5. Liu Y, Xiao W, Wang S, Chan CWH. Evaluating the direct economic burden of health care-associated infections among patients with colorectal cancer surgery in China. *Am J Infect Control*. 2018;46(1):34-38.
6. Feldman S, Webster RG, Sugg M. Influenza in children and young adults with cancer. 20 cases. *Cancer*. 1977;39(1):350-353.
7. IASR 40(11), 2019 [THE TOPIC OF THIS MONTH] Influenza 2018/19 season, Japan [Internet]. [cited 2020 May 1]. Available from: <https://www.niid.go.jp/niid/en/2019-10-04-07-17-22/865-iasr/9288-477te.html>
8. Cooksley CD, Avritscher EBC, Bekele BN, Rolston KV, Geraci JM, Elting LS. Epidemiology and outcomes of serious influenza-related infections in the cancer population. *Cancer*. 2005;104(3):618-628.
9. Pollyea DA, Brown JMY, Horning SJ. Utility of influenza vaccination for oncology patients. *J Clin Oncol*. 2010;28(14):2481-2490.
10. Demicheli V, Jefferson T, Ferroni E, Rivetti A. Vaccines for preventing influenza in healthy adults (Review) - Summary of findings for the main comparison. *Cochrane Database Syst Rev*. 2018;2:1-254.
11. Earle CC. Influenza vaccination in elderly patients with advanced colorectal cancer. *J Clin Oncol*. 2003;21(6):1161-1166.
12. Blanchette PS, Chung H, Pritchard KI, et al. Influenza vaccine effectiveness among patients with cancer: A population-based study using health administrative and laboratory testing data from Ontario, Canada. *J Clin Oncol*. 2019;37(30):2795-2804.
13. Loulergue P, Mir O, Alexandre J, Ropert S, Goldwasser F, Launay O. Low influenza vaccination rate among patients receiving chemotherapy for cancer. *Ann Oncol*. 2008;19(9):1658.
14. Vinograd I, Baslo R, Eliakim-Raz N, et al. Factors associated with influenza vaccination among adult cancer patients: a case-control study. *Clin Microbiol Infect*. 2014;20(9):899-905.
15. Sekimoto M, Asai A, Ohnishi M, et al. Patients' preferences for involvement in treatment decision making in Japan. *BMC Fam Pract*. 2004;5:1-10.
16. Grohskopf LA, Alyanak E, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: Recommendations of the advisory committee on immunization practices-United States, 2020-21 influenza season. *MMWR Recomm Rep*. 2020;69(8):1-24.
17. Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis*. 2014;58(3):e44-e100.
18. Vollaard A, Schreuder I, Slok-Raijmakers L, Opstelten W, Rimmelzwaan G, Gelderblom H. Influenza vaccination in adult patients with solid tumours treated with chemotherapy. *Eur J Cancer*. 2017;76:134-143.
19. Bitterman R, Eliakim-Raz N, Vinograd I, Zalmanovici Trestioreanu A, Leibovici L, Paul M. Influenza vaccines in immunosuppressed adults with cancer. *Cochrane Database Syst Rev*. 2018.2:1-45 CD008983. <https://doi.org/10.1002/14651858.CD008983.pub3>.
20. Melcher L. Recommendations for influenza and pneumococcal vaccinations in people receiving chemotherapy. *Clin Oncol*. 2005;17(1):12-15.
21. Ortbals DW, Liebhaber H, Presant CA, Amburg V, Illrd AL, Lee JY. Influenza immunization of adult patients with malignant diseases. *Ann Intern Med*. 1977;87(5):552-557.
22. Wumkes ML, Van Der Velden AMT, Los M, et al. Serum antibody response to influenza virus vaccination during chemotherapy treatment in adult patients with solid tumours. *Vaccine*. 2013;31(52):6177-6184.
23. Keam B, Kim MK, Choi Y, et al. Optimal timing of influenza vaccination during 3-week cytotoxic chemotherapy cycles. *Cancer*. 2017;123(5):841-848.
24. Sommer AL, Wachel BK, Smith JA. Evaluation of vaccine dosing in patients with solid tumors receiving myelosuppressive chemotherapy. *J Oncol Pharm Pract*. 2006;12(3):143-154.

25. Arrowood JR, Hayney MS, Mena R, Longtin J. Immunization recommendations for adults with cancer. *Ann Pharmacother*. 2002;36(7-8):1219-1229.
26. Robertson JD, Nagesh K, Jowitt SN, et al. Immunogenicity of vaccination against influenza, *Streptococcus pneumoniae* and *Haemophilus influenzae* type B in patients with multiple myeloma. *Br J Cancer*. 2000;82(7):1261-1265.
27. Molinari NAM, Ortega-Sanchez IR, Messonnier ML, et al. The annual impact of seasonal influenza in the US: Measuring disease burden and costs. *Vaccine*. 2007;25(27):5086-5096.
28. Anderson H, Petrie K, Berrisford C, Charlett A, Thatcher N, Zambon M. Seroconversion after influenza vaccination in patients with lung cancer. *Br J Cancer*. 1999;80(1-2):219-220.
29. Brydak LB, Guzy J, Starzyk J, Machała M, Gózdź SS. Humoral immune response after vaccination against influenza in patients with breast cancer. *Support Care Cancer*. 2001;9(1):65-68.
30. Shildt RA, Luedke DW, Laham MN, Kasai G, El-Beheri S. Antibody response to influenza immunization in adult patients with malignant disease. *Cancer*. 1979;44(5):1629-1635.
31. Del Porto F, Laganà B, Biselli R, et al. Influenza vaccine administration in patients with systemic lupus erythematosus and rheumatoid arthritis: Safety and immunogenicity. *Vaccine*. 2006;24(16):3217-3223.
32. Chalmers A, Scheifele D, Patterson C, et al. Immunization of patients with rheumatoid arthritis against influenza: A study of vaccine safety and immunogenicity. *J Rheumatol*. 1994;21(7):1203-1206.
33. Abu-Shakra M, Press J, Varsano N, et al. Specific antibody response after influenza immunization in systemic lupus erythematosus. *J Rheumatol*. 2002;29(12):2555-2557.
34. Holvast B, Huckriede A, Wilschut J, et al. Safety and efficacy of influenza vaccination in systemic lupus erythematosus patients with quiescent disease. *Ann Rheum Dis*. 2006;65(7):913-918.
35. Maloney DG, Grillo-López AJ, White CA, et al. IDEC-C2B8 (rituximab) anti-CD20 monoclonal antibody therapy in patients with relapsed low-grade non-Hodgkin's lymphoma. *Blood*. 1997;90(6):2188-2195.
36. McLaughlin P, Grillo-López AJ, Link BK, et al. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: Half of patients respond to a four-dose treatment program. *J Clin Oncol*. 1998;16(8):2825-2833.
37. Bedognetti D, Zoppoli G, Massucco C, et al. Impaired Response to Influenza Vaccine Associated with Persistent Memory B Cell Depletion in Non-Hodgkin's Lymphoma Patients Treated with Rituximab-Containing Regimens. *J Immunol*. 2011;186(10):6044-6055.
38. Ljungman P, Nahi H, Linde A. Vaccination of patients with haematological malignancies with one or two doses of influenza vaccine: A randomised study. *Br J Haematol*. 2005;130(1):96-98.
39. Takata T, Suzumiya J, Ishikawa T, Takamatsu Y, Ikematsu H, Tamura K. Attenuated antibody reaction for the primary antigen but not for the recall antigen of influenza vaccination in patients with non-Hodgkin B-cell lymphoma after the administration of rituximab-CHOP. *J Clin Exp Hematop*. 2009;49(1):9-13.
40. Chong CR, Park VJ, Cohen B, Postow MA, Wolchok JD, Kamboj M. Safety of inactivated influenza vaccine in cancer patients receiving immune checkpoint inhibitors. *Clin Infect Dis*. 2020;70(2):193-199.
41. Läubli H, Balmelli C, Kaufmann L, et al. Influenza vaccination of cancer patients during PD-1 blockade induces serological protection but may raise the risk for immune-related adverse events. *J Immunother Cancer*. 2018;6(1):1-10.
42. Wijn DH, Groeneveld GH, Vollaard AM, et al. Influenza vaccination in patients with lung cancer receiving anti-programmed death receptor 1 immunotherapy does not induce immune-related adverse events. *Eur J Cancer*. 2018;104:182-187.
43. Kroon FP, Van Dissel JT, De Jong JC, Zwiderman K, Van Furth R. Antibody response after influenza vaccination in HIV-infected individuals: A consecutive 3-year study. *Vaccine*. 2000;18(26):3040-3049.
44. Miotti PG, Nelson KE, Dallabetta GA, Farzadegan H, Margolick J, Lou CM. The influence of HIV infection on antibody responses to a two-dose regimen of influenza vaccine. *J Am Med Assoc*. 1989;262(6):779-783.
45. Welliver R, Monto AS, Hassman M, et al. Effectiveness of Oseltamivir in preventing. *JAMA*. 2001;285(6):748-754.
46. Casper C, Englund J, Boeckh M. How I treat influenza in patients with hematologic malignancies. *Blood*. 2010;115(7):1331-1342.
47. Uehara T, Hayden FG, Kawaguchi K, et al. Treatment-emergent influenza variant viruses with reduced baloxavir susceptibility: impact on clinical and virologic outcomes in uncomplicated influenza. *J Infect Dis*. 2020;221(3):346-355.
48. Ikematsu H, Hayden FG, Kawaguchi K, et al. Baloxavir Marboxil for Prophylaxis against Influenza in Household Contacts. *N Engl J Med*. 2020;383(4):309-320.
49. Goossen GM, Kremer LCM, van de Wetering MD. Influenza Vaccination In Children Being Treated With Chemotherapy For Cancer. *Cochrane Database Syst Rev*, Vol. 2013; 2013(8):CD006484. <https://doi.org/10.1002/14651858.CD006484.pub3>.

How to cite this article: Maeda T, Sasaki H, Togawa A, et al. Surveillance of the current situation regarding influenza vaccination according to medical oncologists in Japan. *Cancer Sci*. 2021;112:433-443. <https://doi.org/10.1111/cas.14742>